

hepatitis B virus is already fraught with difficulties. A good response (>100 mU antibodies to hepatitis B surface antigen/ml) is achieved in only 76.4% of adults and is less likely with increasing age; the vaccine is expensive, and uptake among health service workers is low.⁶ These problems must not be compounded by use of an inappropriate site of injection.

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Too deep or not deep enough?

EDITOR,—The 11 July issue of the *BMJ* makes intriguing reading, not least the correspondence column. Richard Park and Peter R Mills are upset that critics "did not read our study more carefully,"¹ while Ian Forgacs suggests that another critic "may have read our editorial rather too closely."² In the news section Linda Beecham announces the launch of the *Student BMJ*; one of its aims is to encourage the reading of scientific papers.³ Perhaps the *Student BMJ*'s recommendations for the required depth of study per article should be shared with the *BMJ*'s readers.

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Outcome in the chronic fatigue syndrome

EDITOR,—Michael Sharpe and colleagues' paper confirms what many clinicians have long suspected—namely, that the prognosis for those with a chronic fatigue syndrome who reach specialist care is poor.¹ The paper also suggests that membership of a self help organisation is associated with a poor outcome. Although the authors emphasise that this association is not necessarily causal, I fear that the self help organisations may interpret this as another attack on their credibility, which will further sour relations between the organisations and the profession.

What are the possible explanations for these disturbing findings? Sharpe and colleagues suggest that patients' beliefs are an important mediator of disability, a view I share.² An article written by a sufferer illustrates how this might happen: "These living viruses are erratic and unpredictable. The prickly-edged ones pierce their way into the body cells. If disturbed by the patient's activity they become as aggressive as a disturbed wasps' nest, and can be felt giving needle-like jabs (or

stimulating the nerves to do so)."³ It is easy to understand how such beliefs, regardless of their scientific accuracy, amplify disability.

The situation is rendered more tragic as it now seems that the evidence on which these beliefs (that persistence of enteroviruses in muscles is the cause of undoubtedly genuine symptoms) is based is less than convincing. Previous work on enteroviral serology is now known to be unreliable,⁴ as is the finding of persistent enteroviral antigenaemia.⁵ Most importantly, it seems increasingly unlikely that this condition results from any neuromuscular disorder, viral or otherwise.⁶ I hope that this more optimistic research will be publicised with the same vigour that greeted previous findings.

Sharpe and colleagues' findings of a poor prognosis should cause all those who advise patients with the chronic fatigue syndrome to pause for thought and perhaps discard cherished beliefs. Members of the medical profession should also rethink their attitudes towards sufferers as, clearly, neither the profession nor the self help organisations are effective at relieving disability.

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EDITOR,—Michael Sharpe and colleagues' follow up study of 177 patients with chronic fatigue of uncertain origin raises several important unanswered questions, which require further investigation.¹ Factors such as a belief that their illness followed an infection, intolerance to alcohol, and membership of a support group for patients with myalgic encephalomyelitis were all associated with an adverse prognosis. Could it be that the authors had identified patients belonging to a distinct postinfectious subgroup as many doctors maintain they do? Clearly, if this is the case future studies of this nature will have to include more objective analysis of persisting viral infection (for example, analysis of muscle biopsy specimens with the polymerase chain reaction rather than tests for VP1 antigen); immune function (for example, function of natural killer cells rather than white cell counts); and hypothalamic-pituitary-axis activity (for example, up regulation of serotonin-1 receptors and basal cortisol concentrations) to see if there are characteristic abnormalities that distinguish the postinfectious subgroup.

The high incidence of intolerance to alcohol is noted as intriguing, but from personal experience, as well as from seeing many patients with a classic postinfectious fatigue syndrome, I regard this observation as an important diagnostic feature. In these patients even small amounts of alcohol cause a further deterioration in cognitive function, and I suggest that a physiological explanation may lie in the fact that alcohol increases the concentration of the neurotransmitter γ -aminobutyric acid, which in turn reduces the availability of calcium ions and hence depresses brain function still further.²

The observation that four of 55 patients had greatly improved, and a further 13 were worse, as a result of antidepressant treatment also brings into question Sharpe's recent conclusion "that such patients may be suffering from a depressive

illness, of which physical fatigue is a somatic manifestation."³ Although these drugs clearly have a role in patients with coexistent depression, a much larger survey of 336 patients found that, overall, they were no more effective than therapeutic nonsense such as a regimen to eliminate candida.⁴

The problem with any kind of research into the chronic fatigue syndrome is that, like backache, it covers a large heterogeneous group of patients in whom physical, psychological, and social factors may be interacting. Researchers should therefore not be surprised to find that the outcome varies considerably when the aetiology is not more clearly defined.

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EDITOR,—Michael Sharpe and colleagues report that most patients with the chronic fatigue syndrome rate contact with medical services as unhelpful or only slightly helpful.¹ Many sufferers turn to alternative health care, again with varied success. Such dissatisfaction with medical care is well documented,² and self help organisations flourish to provide the support, advice, and education that is not, or cannot be, provided by the medical profession; they potentially fulfil an important role.

The authors conclude that for patients with the chronic fatigue syndrome membership of a self help organisation is associated with a poorer outcome (although whether members were more functionally impaired at the outset is not known). Adopting coping strategies, particularly with regard to exercise and "stress," and a belief in the persistence of a viral infection are also associated with continuing disability.

Unfortunately, such advice continues to be offered to patients with the syndrome, particularly by self help organisations. It is to be hoped that all those caring for patients will take note of Sharpe and colleagues' conclusions. Work with fatigued patients in primary care (E McDonald *et al*, paper in preparation) suggests that general practitioners have a central role in preventing the longer term secondary disability described by the authors—by acknowledging the distress caused by fatigue, limiting investigations and referrals to specialist centres, prescribing antidepressants when appropriate, and encouraging maintenance of activities. The patients in Sharpe and colleagues' study were receiving secondary care, and possibly by then beliefs and attitudes to physical symptoms are already engrained.

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Dangers of aspirin before cardiac surgery

EDITOR,—In the final paragraph of his editorial Stuart M Cobbe states, "The outcomes of ISIS-3 and GISSI-2 have resulted in a policy of no change and a sigh of relief from most British doctors and